Rodbell Impact

A Far Ranging Impact

Researchers have discovered hundreds of different receptors that act through G-proteins—Rodbell's transducer molecules. More than 65% of all prescription drugs act on such receptors, and a significant portion of the human genome codes for these receptors. Defective G-proteins cause a number of diseases.

> *"When we know the whole diagram [of signal transduction in all types of cells], we'll know how every cell is controlled. You'll be able to design a drug that works only on the molecule you want and on no other molecule in the body. It will happen. I just can't tell you when."*
>
> - *–Alfred G. Gilman*

Work continues as researchers attempt to identify and determine the structure of all the body's receptors and to clarify the role they play in normal functions like human growth, detecting light and odor, and in fighting infection. Here are just three conditions where G-proteins are important:

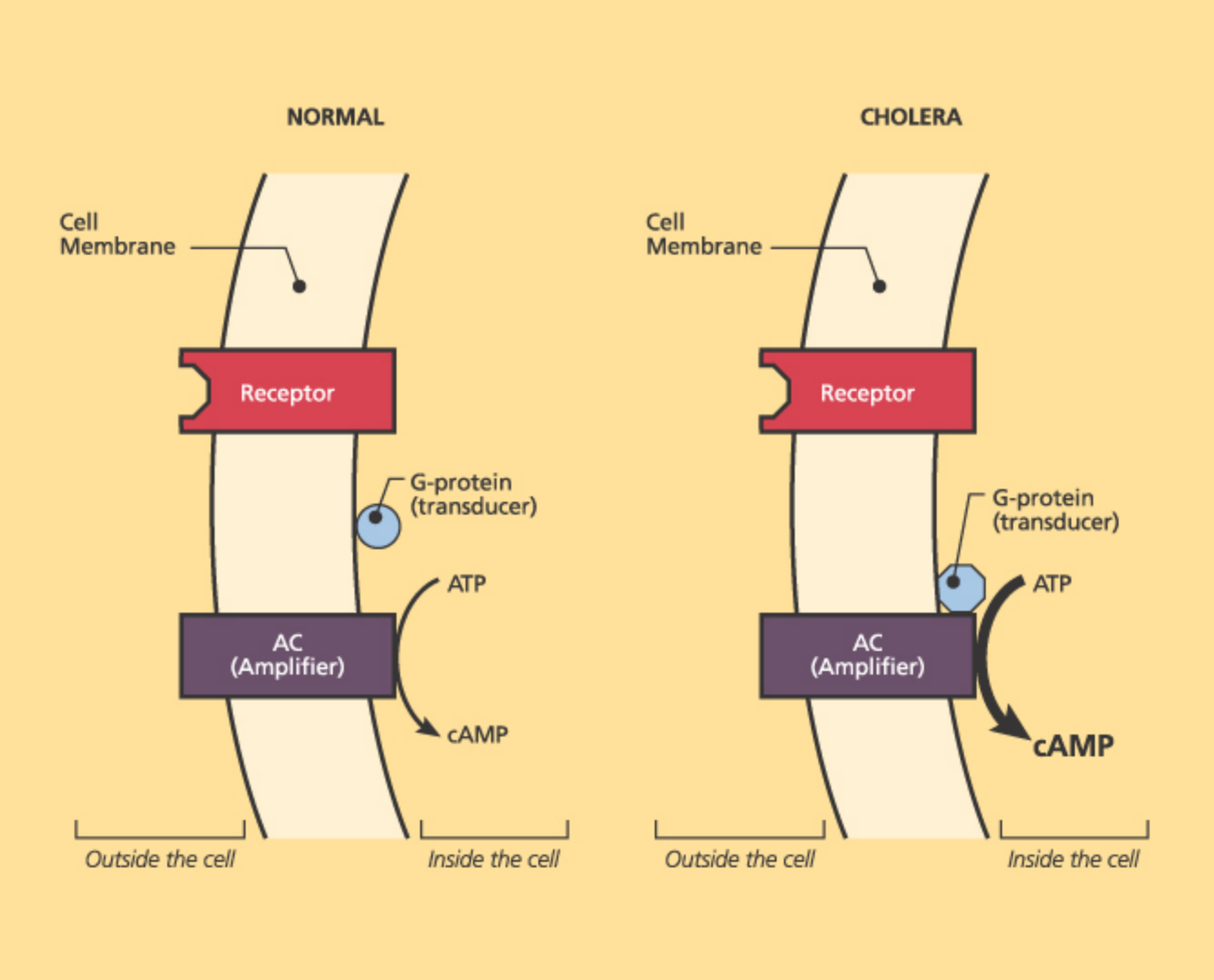
Cholera

Cholera is an infectious disease that spreads in countries without clean drinking water or adequate sewage disposal. The bacterium causing the disease was identified in 1884. How it causes disease was discovered almost 100 years later.

A toxin produced by the bacterium changes the G-proteins in cells lining the intestine. The G-proteins become "stuck" in the activated—or turned on—state. They can't turn themselves off as they do when normally regulated. The effect is that water is pumped continuously out of the cells into the intestines, causing dangerously severe diarrhea.

About the Diagram

Normally, both the receptor and the amplifier span the membrane. The G-protein sits on the inner surface of the membrane. This current view is a little different from Rodbell's original model. In a person with cholera, the G-protein is stuck in the "on" position-next to the AC molecule



What Causes Cholera Image: Courtesy of NIDDK

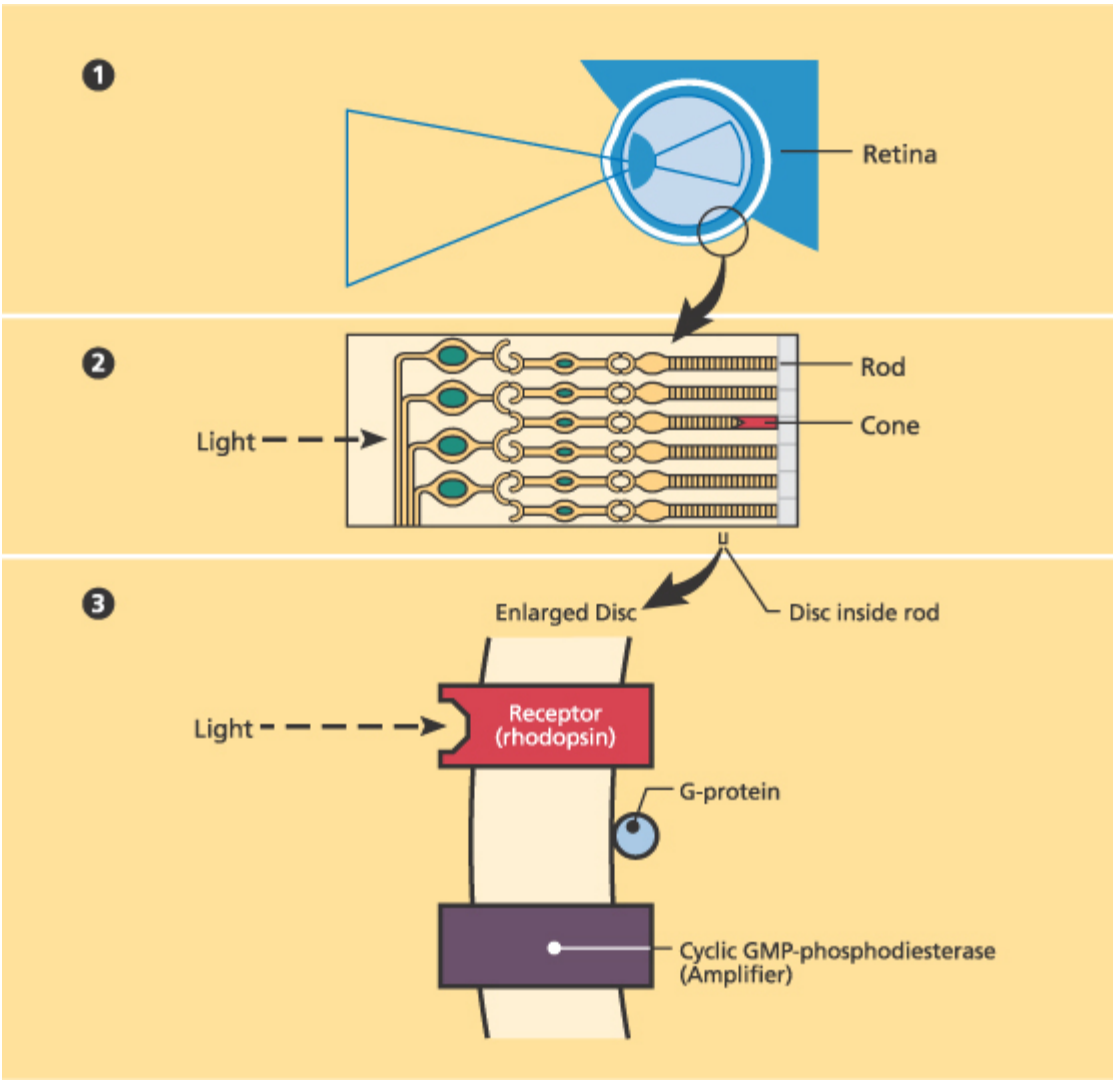
Inherited Night Blindness

Scientists have found a G-protein defect in one type of inherited night blindness. Persons with this condition have a mutation in the gene that codes for the G-protein found in the eye's rod cells. Scientists believe that this defective G-protein is overactive. It stays turned on more than it normally would, and the person can't see well at low light levels.

During the day, a similar system in the cone cells of the eyes allows us to see color. This system depends on a different G-protein. Thus, persons with night blindness have normal daytime vision.

About the Diagram

When light strikes a light receptor, it activates a G-protein, which binds to an amplifier molecule. This sends a signal to the brain, resulting in light perception. G-proteins normally turn themselves off in a natural regulatory cycle. But in inherited night blindness, the G-protein stays on, interfering with normal vision.



Light enters the eye (1) and strikes the rod cells in the retina (2). Light receptors, G-proteins and amplifiers are on discs within the rods (3) Image : Courtesy of NIDDK

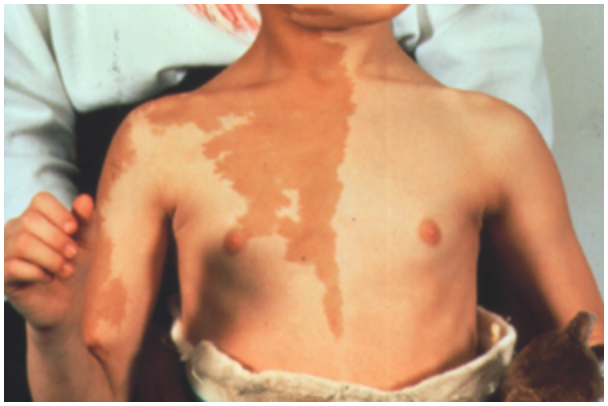
McCune Albright Syndrome

McCune Albright syndrome is an unusual type of disease with varied symptoms. In this disease, a mutation occurs sometime after conception, affecting only some of the body's cells. The number and type of symptoms depend on which cells—and thus which organs—are affected.

Scientists have found that the mutation affects the gene that codes for he same G-protein involved in cholera. This G-protein gets stuck in the "on" position. In skin cells, this causes darker than normal pigment. If the mutation affects bone cells, it causes weakness and fractures. In hormone-producing cells, the mutation causes the release of excess hormones.

About the Photo:

Skin cells and bone cells are affected in this 4-year-old girl with McCune Albright syndrome. She wears a body cast because of bone fractures. The mosaic pattern of darkened skin is visible.



McCune Albright syndrome Courtesy of the Developmental Endocrinology Branch, NICHD
The 1994 Nobel Prize